Remarks

Upon entry of the foregoing amendments, claims 37 – 56 are under consideration.

THE §101 REJECTION

The Examiner has rejected claims 37 – 56 under 35 U.S.C. §101, alleging that the claimed invention has no apparent or disclosed specific and substantial credible utility, as the instant Application does not disclose the biological role of the claimed protein/DNA or its significance.

Applicants traverse. Applicants respectfully submit that the rejection is contrary to both the law and the United States Patent Office's own examination guidelines. The Examiner has based her rejection on MPEP 2107.03. Applicants contend that the Examiner has not cited the entire rule from MPEP 2107.03. In the MPEP, "close" structural similarity, and "evidence demonstrating substantial activity of the claimed compounds" are part of a case for establishing utility; however, from a reading of the rest of the passage, the MPEP further reports that

> Such evidence should be given appropriate **weight** in determining **whether one skilled in the art would find the asserted utility credible**.

MPEP 2107.03(I) (2004). From this wording, it is clear that homology and pharmacological activity are not elements, both requiring a minimum quantum of proof to support the ultimate finding of utility. Rather, homology and pharmacological activity are factors whose weights are determined by what a person having ordinary skill in the art would recognize as utility. Each of these factors are individually addressed below.

Homology

The Examiner contends that Zins4 lacks exclusive homology to relaxin; that Zins4 has homology to both insulin and relaxin; and therefore, it is not clear whether Zins4 will behave like insulin, like relaxin, or like something else.

Applicants traverse. Applicants contend that the Office has not established a *prima facie* showing for lack of utility, because Applicants have asserted a clear homology to relaxin

specifically by giving a factual basis for this assertion such that one having ordinary skill in the art would recognize Zins4's homology to relaxin.

As stated in the Specification, the polypeptides of the present invention have "homology to the relaxin family." *See e.g.* Specification at pg. 9, lines 13-15. Specifically, these polypeptides share numerous structural similarities with the hormone relaxin. For instance, the polypeptides of the present invention contain a B Chain-C peptide-A chain motif found in relaxins. *Id* at pg. 9, line 36 through pg 10., line 1. More specifically, the polypeptides of the present invention share a classic relaxin structure, known as the "cysteine motif," which is highly conserved in the B and A chains of relaxin. *Id* at pg 9, lines 27-35. In fact, "[s]equence analysis indicates that the human polypeptide sequence (SEQ ID NO: 2) is structurally equivalent to other members of the [relaxin] family." *Id* at pg. 10, lines 5-6. Further, the length of the B Chain, C peptide and A chain correspond closely to relaxin itself. *Id* at pg. 10, line 7 through pg. 11, line 14. The presence of these structural similarities would lead one of ordinary skill in the art to conclude that the polypeptides of the present invention are closely related to relaxin.

Most importantly, the Applicants have cited material that shows not only that one having ordinary skill in the art would recognize Zins4's homology to relaxin, but that **one having ordinary skill in the art has recognized Zins4's homology to relaxin**. The polypeptides of the present invention contain an R-x-x-x-R-x-x-I motif in the middle of the B-chain (starting at amino acid residue 37 (Arg) through residue 44 (Ile) of SEQ ID NO: 2). This motif has been determined to be "**essential for relaxin binding**." *See e.g.*, Bethgate *et al.*, *J. Bio. Chem.* 227:2 1148-1157 (2001) (cited in the June 12, 2002 Information Disclosure Statement as reference "A3") (*emphasis added*); *see also*, Specification at pg. 9, lines 31-35. In fact, **Zins4 and relaxin *alone* share this B chain motif**. The polypeptides of the present invention are homologous to relaxin and consequently are more likely than not to have a substantially similar biological function as relaxin, as these structural characteristics are well known in the art and are recognized as defining and directing relaxin's biological function(s).

Pharmacological Activity

The Examiner further contends that Applicants cannot show that Zins4 has pharmacological activity through its homology with relaxin; noting 1) that, Applicants have disclosed several divergent uses for Zins4 and 2) that Applicants' disclosure of relaxin homology is insufficient to show utility because "Many protein [sic] may share receptor binding regions, but proteins which are agonists and antagonists of the same receptor frequently share binding motifs."

Applicants assert that Zins4 has a unified activity, directly related to female reproductive tract physiology such that one having ordinary skill in the art would recognize its utility. Applicants respectfully direct the Examiner to the similarity between the current Application and the Application in *In re Gardner*. *In re Gardner* found that there was substantial utility where the Applicant had claimed a set of compounds with an admittedly divergent set of specific activities but an overall unified activity. *In re Gardner*, 475 F.2d 1389, 177 USPQ (BNA) 396 (C.C.P.A. 1973). To illustrate, the Gardner Specification states that "some of the compounds... have very pronounced adrenergic nerve blocking activity" and "some... have pronounced ganglion blocking activity and antihistaminic activity". *Id* at 1392. The Court's finding of utility was based on an analysis of whether the "ganglion blocking activity [was] merely another mechanism for achieving the antihypersensive effect." Thus, to find substantial utility, the Court considered whether there was a unified single activity and upon finding a unified activity, the Court found that there was substantial utility. *Id.*

Similarly, as the Examiner has described in the February 25th, 2004, Final Rejection, Applicants have disclosed a number of uses for the various incarnations of Zins4; however, the Applicants assert a unified activity. Applicants assert that Zins4 exhibits the unified activity of contractility of tissues, such as myometrial tissues, in the female reproductive tract physiology. In support of this unified activity and the specificity of Zins4's binding regions Applicants point to the present invention's similarity to relaxin, which is known to exhibit the same activities. Applicants have disclosed a specific motif (namely the R-x-x-x-R-x-x-I motif) and a source connecting this motif *exclusively* with relaxin. The R-x-x-x-R-x-x-I motif expressed in the B-chain has been determined to be "**essential for relaxin receptor binding.**" *See e.g.*, Bethgate *et*

al., *supra*, at 1148-1157. In fact **Zins4 and relaxin *alone* share this B chain motif**. As such one having ordinary skill in art would and has recognized the specific activity of Zins4.

To further substantiate Applicants' assertion of utility for Zins4, Applicants would call the Examiner's attention to the decision of the United States Court of Customs and Patent Appeals in *Nelson v. Bowler*:

> The applicant does not have to prove that a correlation exists between a particular activity and an asserted therapeutic use of a compound as a matter of statistical certainty, nor does he or she have to provide actual evidence of success in treating humans where such a utility is asserted. Instead, as the courts have repeatedly held, all that is required is a reasonable correlation between the activity and the asserted use.

MPEP 2107.03(I)(2004) citing *Nelson v. Bowler*, 626 F.2d 853, 857, 206 USPQ 881, 884 (CCPA 1980). As an extension of *Nelson*, as *Nelson*'s showing of pharmacological activity constituted a showing of practical utility even though he did not disclose a therapeutic utility, so all of the biological data that we show such as expression data, chromosome localization, and binding regions, constitutes a showing of practical utility even if Applicants do not disclose a specific therapeutic or diagnostic application. Applicants contend that disclosures in the specification showing structural similarity to relaxin and further reference to the Bethgate article, showing exclusivity of the R-x-x-x-R-x-x-I to Zins4 and relaxin, have shown a "reasonable correlation between the activity and the asserted use." *Id.*

Based on the foregoing discussion, it is clear that the Examiner's assertion that Zins4 lacks homology to relaxin specifically and that Zins4 has no substantiated pharmacological activity is unfounded. The weight of evidence supporting both of these factors is sufficient such that one having ordinary skill in the art would find the asserted utility to be credible. The Office has not established a *prima facie* showing of lack of utility, nor sound scientific reasoning to rebut the assertions of utility in this Application. As a result, Applicants request that the Examiner withdraw the present rejection under 35 U.S.C. §101.

THE §112, FIRST PARAGRAPH REJECTION

The Examiner has rejected claims 37 – 56 under 35 U.S.C. §112, first paragraph, alleging that the Specification fails "to adequately teach how to use the instant invention for the reasons given above with regard to the rejection of [the] claims under 35 U.S.C. 101."

Applicants traverse. Applicants have indeed taught how to use the instant invention. As discussed above, Applicants have shown that the polypeptides of the present invention share numerous structural similarities with relaxin and, in fact, have been classified by those skilled in the art as being relaxins. Consequently, Applicants have shown a biological activity for the polypeptides of the present invention. Thus, Applicants assert that the Specification more than adequately teaches how to use the present invention.

Accordingly, Applicants maintain that they have indeed asserted a specific and substantial credible utility and well-established utility for the claimed polypeptides. The Zins4 polypeptides of the present invention are useful, and therefore one of skill in the art could make and use the invention. Consequently, Applicants request that the Examiner withdraw the rejection of claim 11 under 35 U.S.C. §112, first paragraph.

CONCLUSION

On the basis of the foregoing amendments and remarks, Applicants respectfully submit that the pending claims are in condition for allowance. If for any reason the Examiner feels that a telephone conference would expedite prosecution of the Application, the Examiner is encouraged to contact the undersigned at the telephone number provided below.

Respectfully submitted,

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Enclosures:

Petition and Fee for Extension of Time (in duplicate)
Amendment Fee Transmittal (in duplicate)
Postcard

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